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(54) Title of the Invention
Stable dantrolene sodium preparation

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Specification

1. Title of Invention: Stable dantrolene sodium preparation

2. What is claimed is:

(1) A stable dantrolene sodium preparation wherein 1, or 2 or more salts selected from the group comprising normal and hydrogen alkali metal salts are mixed within a 1 – { [5 – (p-Nitrophenyl) furfurylidene] amino} hydantoin sodium hydrate (hereinafter referred to as "dantrolene sodium") in suspension so that the pH of the solution is 9-11.

(2) A stable dantrolene sodium preparation according to claim 1 in the form of a dry syrup or suspension.

3. Detailed Description of the Invention

The present invention concerns a stable dantrolene sodium preparation combined with 1, or 2 or more salts selected from the group comprising normal and hydrogen alkali metal salts.

Dantrolene sodium is a durable skeletal muscle relaxant having a hydantoin ring, it is an extremely useful drug for counteracting skeletal muscle twitching etc. caused by diseases of the central nervous system and spinal cord.

However, when dantrolene sodium is suspended in water it quickly becomes unstable and the hydantoin ring shown in the formula below, which is subject to rapid hydrolysis, opens. This activity is therefore a weak point.

[formula]

Dantrolene sodium

Therefore, as a result of the inventors' varied research into preventing the breakdown of dantrolene sodium, they discovered the present invention wherein 1, or 2 or more salts selected from the group comprising normal and hydrogen alkali metal salts are added to dantrolene sodium to prevent the breakdown of dantrolene sodium within a solution.

The normal alkali metal salts used in the present invention are those that are pharmaceutically permissible, for example sodium citrate, sodium succinate, potassium tartrate, sodium malate, sodium chloride, potassium chloride etc. The hydrogen alkali metal salts used in the present invention may be, for example, sodium bicarbonate, disodium hydrogen phosphate, dipotassium hydrogen phosphate.

The proportion in which the dantrolene sodium and alkali metal salts are mixed together in the preparation of the present invention is as follows: in 1 ml of solution, 1-50 mg, but preferably 2-30 mg alkali metal salts per 1-50 mg of dantrolene sodium, to a pH of 9-11. The preparation of the present invention can be made up as a liquid

suspension, and for oral administration as a liquid preparation it may be made into a powder or granule syrup (meaning a ready-to-use syrup suspension).

The following is an embodiment showing the stable effect of the present invention.

Embodiment: A brown syrup bottle was filled with each of the following suspensions, and after being stored at 40°C for 7 days, the remaining dantrolene sodium was separated by thin layer chromatography for analysis and measured by photo absorption method.

	Formulation	Amount (mg/ml)	pH at time of formulation	Remaining rate (%)
A	Dantrolene sodium	5.0	10.2	70.4
B	Dantrolene sodium Sodium citrate	5.0 8.5	9.6	98.2
C	Dantrolene sodium Potassium tartrate	5.0 11.3	10.0	92.4
D	Dantrolene sodium Sodium succinate	5.0 8.1	9.6	99.7
E	Dantrolene sodium Sodium chloride	5.0 5.8	9.3	98.4

As clearly shown by these results, the present invention sufficiently prevents the hydrolysis of dantrolene sodium.

Furthermore, as the present invention is for ordinary oral administration, sweeteners such as sucrose, mannitol and sorbitol, suspenders such as sodium carboxymethyl cellulose and methyl cellulose, binders such as hydroxypropyl cellulose and polyvinylpyrrolidone, preservatives such as methylparaben and propylparaben, food colourings and other colouring agents, aromas, and surfactants such as polyoxyethylene stearate (polyoxyl (40) stearate) and polyoxyethylene sorbitan monooleate (polysorbate 80) can be added.

Embodiment 1

25 g sucrose, 850 mg sodium citrate and 200 mg methylparaben were dissolved in purified water, 500 mg of dantrolene sodium was suspended within the solution and purified water added to a total volume of 100 ml.

Embodiment 2

25 g sucrose, 1.13 g potassium tartrate and 200 mg methylparaben were dissolved in purified water, 500 mg of dantrolene sodium was suspended within the solution and purified water added to a total volume of 100ml.

Embodiment 3

25g sucrose, 810 mg sodium succinate, 200 mg methylparaben and 1g sodium carboxymethyl cellulose were dissolved in purified water, 500 mg of dantrolene

sodium was suspended within the solution and purified water added to a total volume of 100 ml.

Embodiment 4

25 g sucrose, 580 mg sodium chloride and 200 mg methylparaben were dissolved in purified water, 500 mg of dantrolene sodium was suspended within the solution and purified water added to a total volume of 100ml.

Embodiment 5

500 mg of dantrolene sodium, 850 mg sodium citrate, 200 mg methylparaben and 23.3 g powdered sugar were combined in a preparation and 150 mg hydroxypropyl cellulose added to form granules. 100 ml of water was added to this granule preparation.

Kouichi Sasaki, Patent Attorney